

Internal Application No PC1/EP2004/051522

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K39/108 A61F A61K39/112 C07K14/25 C07K14/245 According to international Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 **CO7K** Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, CHEM ABS Data, MEDLINE, WPI Data, PAJ, EMBASE C. DOCUMENTS CONSIDERED TO BE RELEVANT Category 9 Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X SHEORAN ABHINEET S ET AL: "Stx2-specific 17 human monoclonal antibodies protect mice against lethal infection with Escherichia coli expressing Stx2 variants. INFECTION AND IMMUNITY. JUN 2003, vol. 71, no. 6, June 2003 (2003-06), pages 3125-3130, XP002301428 ISSN: 0019-9567 page 3125, right-hand column, paragraph 2 - page 3126, right-hand column, paragraph 5; figure 1 -/--X Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance Invention \*E\* earlier document but published on or after the International "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another "Y" document of particular relevance: the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled \*O\* document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but in the art. later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 19 October 2004 08/11/2004 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Steffen, P Fax: (+31-70) 340-3016





2 42		PC1/EP2004/051522			
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X	MACLEOD D L ET AL: "Purification and characterization of an Escherichia coli Shiga-like toxin II variant." INFECTION AND IMMUNITY. MAY 1990, vol. 58, no. 5, May 1990 (1990-05), pages 1232-1239, XP002301430 ISSN: 0019-9567 page 1234, left-hand column, paragraph 2 paragraph 3 page 1236, left-hand column, paragraph 2; figure 4	17			
X	DOWNES F P ET AL: "Affinity purification and characterization of Shiga-like toxin II and production of toxin-specific monoclonal antibodies."  INFECTION AND IMMUNITY. AUG 1988, vol. 56, no. 8, August 1988 (1988-08), pages 1926-1933, XP002923370  ISSN: 0019-9567 page 1927 - page 1930; figure 7	17			
X	BELISLE B W ET AL: "Monoclonal antibodies with an expanded repertoire of specificities and potent neutralizing activity for Escherichia coli heat-labile enterotoxin."  INFECTION AND IMMUNITY. DEC 1984, vol. 46, no. 3, December 1984 (1984-12), pages 759-764, XP002301431  ISSN: 0019-9567 page 759 - page 760; table 1	17			
X	BELISLE B W ET AL: "Characterization of monoclonal antibodies to heat-labile enterotoxin encoded by a plasmid from a clinical isolate of Escherichia coli." INFECTION AND IMMUNITY. MAR 1984, vol. 43, no. 3, March 1984 (1984-03), pages 1027-1032, XP002301432 ISSN: 0019-9567 page 1027 - page 1028; table 1	17			



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C.(Continu Category *	ction) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
A	JEMAL C ET AL: "Analysis of Shiga toxin subunit association by using hybrid A polypeptides and site-specific mutagenesis."  JOURNAL OF BACTERIOLOGY. JUN 1995, vol. 177, no. 11, June 1995 (1995-06), pages 3128-3132, XP000669314 ISSN: 0021-9193 page 3128 - page 3129; tables 1,3	1-17		
A	MELTON-CELSA ANGELA R ET AL: "Activation of Shiga toxin type 2d (Stx2d) by elastase involves cleavage of the C-terminal two amino acids of the A2 peptide in the context of the appropriate B pentamer" MOLECULAR MICROBIOLOGY, vol. 43, no. 1, January 2002 (2002-01), pages 207-215, XP002267546 ISSN: 0950-382X page 208, right-hand column, paragraph 2 - page 210, right-hand column, paragraph 1; figures 1-3	1-17		
A	RODIGHIERO CHIARA ET AL: "Structural basis for the differential toxicity of cholera toxin and Escherichia coli heat-labile enterotoxin. Construction of hybrid toxins identifies the A2-domain as the determinant of differential toxicity" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 7, 12 February 1999 (1999-02-12), pages 3962-3969, XP002267547 ISSN: 0021-9258 page 3963, right-hand column, paragraph 3 - page 3964, right-hand column, paragraph 1; figure 1	1-17		
Α	MARTIN M ET AL: "Recombinant antigen-enterotoxin A2/B chimeric mucosal immunogens differentially enhance antibody responses and B7-dependent costimulation of CD4(+) T cells."  INFECTION AND IMMUNITY. JAN 2001, vol. 69, no. 1, January 2001 (2001-01), pages 252-261, XP002231728  ISSN: 0019-9567 page 253 - page 255; figure 1  -/	1-17		

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A 40	-N-N BOOMERIES CONSIDERED TO DE CUE SUSTI	PC1/EF2004/051522		
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A	JOBLING M G ET AL: "Fusion proteins containing the A2 domain of cholera toxin assemble with B polypeptides of cholera toxin to form immunoreactive and functional holotoxin-like chimeras." INFECTION AND IMMUNITY. NOV 1992, vol. 60, no. 11, November 1992 (1992-11), pages 4915-4924, XP002292263 ISSN: 0019-9567 page 4916 - page 4920	1-17		
A	WO 01/70945 A (SIBTECH INC) 27 September 2001 (2001-09-27) figure 1; examples 1-3	1-17		
A	WO 01/89456 A (UNIV TULANE ;CLEMENTS JOHN D (US)) 29 November 2001 (2001-11-29) figure 1; example 6.1	1-17		
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A	MERRITT ETHAN A ET AL: "AB-5 toxins" CURRENT OPINION IN STRUCTURAL BIOLOGY, vol. 5, no. 2, 1995, pages 165-171, XP002267548 ISSN: 0959-440X figures 1,2; table 1	1-17		
A	PATON J C ET AL: "Pathogenesis and diagnosis of Shiga toxin-producing Escherichia coli infections." CLINICAL MICROBIOLOGY REVIEWS. JUL 1998, vol. 11, no. 3, July 1998 (1998-07), pages 450-479, XP002105349 ISSN: 0893-8512 page 469, right-hand column, paragraph 3 page 470, right-hand column, paragraph 3	1-17		
A	LEBENS M ET AL: "Synthesis of hybrid molecules between heat-labile enterotoxin and cholera toxin B subunits: potential for use in a broad-spectrum vaccine." INFECTION AND IMMUNITY. JUN 1996, vol. 64, no. 6, June 1996 (1996-06), pages 2144-2150, XP002301433 ISSN: 0019-9567 the whole document	1-17		

## INTERNATIONAL SEARCH REPURT Information on petent family members

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WO 0170945	A	27-09-2001	US EP JP WO US	2001031485 A1 1268760 A1 2003533980 T 0170945 A1 2004166565 A1	18-10-2001 02-01-2003 18-11-2003 27-09-2001 26-08-2004
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## INTERNATIONAL SEARCH REPORT

mational application No.

PCT/EP2004/051522

Box No. 1	Nucleotide and/or amino acid sequence(s) (Continuation of Item 1.b of the first sheet)
1. With inver	regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed nation, the international search was carried out on the basis of:
a.	type of material  X a sequence listing table(s) related to the sequence listing
b.	format of material  X in written format  X in computer readable form
c.	time of filing/furnishing  X contained in the international application as filed  filed together with the international application in computer readable form  furnished subsequently to this Authority for the purpose of search
2. X	In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Add	Altional comments: